

Investigation of twin screw granulation: integrating experimental and computational approaches

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Efforts towards switching from batch to continuous processing with 24/7 production capacity are one of the major considerations within the pharmaceutical industry to significantly improve its traditional batch manufacturing. However, a transformation to a completely continuous process requires all the unit operations to be performed in continuous mode with inter-compatibility. In this context, twin-screw granulation (TSG) has emerged as a promising product design process for continuous wet granulation in continuous solid dosage manufacturing. A continuous manufacturing line with continuous TSG is followed by a dryer, product control hopper and tableting machine. A TSG achieves mixing and granulation by a complex interplay between the screw configuration and process settings (e.g. feed rate, screw speed, etc.) to produce products with pre-defined end-product specifications in a short time. However, in depth understanding of the complex interplay of processes taking place is required to optimise and control this new technology. To this purpose, a combination of experimental and mathematical techniques/approaches was applied in this study. The characterisation of wetted material transport and mixing inside the confined spaces of rotating screws was performed and the experimental residence times were obtained from near infrared chemical imaging. The experimental data was then compared to a conceptual model based on classical chemical engineering methods to estimate the parameters of the model and to analyse the effects of changes in number of kneading discs and their stagger angle, screw speed and material throughput on residence time. In addition, to understand the granule size distribution (GSD) dynamics as function of individual screw modules along the TSG barrel, the change in GSD was investigated experimentally and mathematically. The experimental data was used for calibrating a population balance model for each kneading disc module in the twin-screw granulator in order to obtain an improved insight into the role of kneading discs at a specified location inside the TSG. The study established that the kneading block in the screw configuration acts as a plug-flow zone inside the granulator. It was found that a balance between the throughput force and conveying rate is required to obtain a good axial mixing inside the twin-screw granulator. Also, a high throughput can be achieved by increasing the liquid-solid ratio and screw speed. Furthermore, the role of the first kneading block after wetting and the second kneading block will be discussed.